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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/051,843	01/17/2002	Kathleen H. Young	AHP 98133 P1	3063

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EXAMINER	
MURPHY, JOSEPH F	
ART UNIT	**PAPER NUMBER**
1646	

DATE MAILED: 02/08/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/051,843	YOUNG ET AL.	
	Examiner	Art Unit	
	Joseph F Murphy	1646	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *24 November 2004*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *45,46,50 and 52-68* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *45,46,50 and 52-68* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Formal Matters

Claims 45-46, 50, 52-68 are pending and under consideration.

Response to Amendment

The rejections of claims 47-49, now cancelled, are rendered moot and thus withdrawn.

The rejection of claims 45-46 under 35 U.S.C. 102(b) as being anticipated by Stephens et al. (1996).

The rejection of claim 50 under 35 U.S.C. 103(a) as being unpatentable over Wang et al. (1996) in view of U.S. Patent No. 6,080,557 (Sims et al.) has been obviated by Applicant's amendment and is thus withdrawn.

Remaining and new issues are set forth below.

Claim Rejections - 35 USC § 112 first paragraph

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 45-46 stand rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a method of evaluating a compound for the ability to inhibit binding of an α-subunit intracellular receptor region of a voltage gated K channel to an amino-terminal inactivation region of a potassium channel protein, wherein the voltage gated channel proteins are Kv1.1 and Kvβ1, does not reasonably provide enablement for a method of evaluating a compound for the ability to inhibit binding of an α-subunit intracellular receptor region of a voltage gated K channel to an amino-terminal inactivation region of a potassium

channel protein, wherein the voltage gated channel proteins are Kv1.1 and Kvβ1 wherein the proteins are biologically active fragments of the proteins, for reasons of record set forth in the Office Action of 8/24/2004. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to practice the invention commensurate in scope with these claims. See In re Wands, 858 F.2d at 737, 8 USPQ2d at 1404. The test of enablement is not whether any experimentation is necessary, but whether, if experimentation is necessary, it is undue.

The rejection of record set forth that the claims are directed to a method of evaluating a compound for the ability to inhibit binding of an α-subunit intracellular receptor region of a voltage gated K channel to an amino-terminal inactivation region of a potassium channel protein, wherein the voltage gated channel proteins are Kv1.1 and Kvβ1 wherein the proteins are biologically active fragments of the proteins. Thus, the claims encompass methods using variant proteins. Applicant has provided little or no guidance beyond the mere presentation of sequence data to enable one of ordinary skill in the art to determine, without undue experimentation, the positions in the protein which are tolerant to change (e.g. such as by amino acid substitutions or deletions), and the nature and extent of changes that can be made in these positions. Although the specification outlines art-recognized procedures for producing and screening for active fragments, this is not adequate guidance as to the nature of active derivatives that may be constructed, but is merely an invitation to the artisan to use the current invention as a starting point for further experimentation. Even if an active or binding site were identified in the specification, they may not be sufficient, as the ordinary artisan would immediately recognize that an active or binding site must assume the proper three-dimensional configuration to be

active, which conformation is dependent upon surrounding residues; therefore substitution of non-essential residues can often destroy activity. Applicants do not disclose any actual or prophetic examples on expected performance parameters of any of the possible fragments of the subunits. It is known in the art that even single amino acid changes or differences in the amino acid sequence of a protein can have dramatic effects on the protein's function, as setf otrh in the previous Office Action. Due to the large quantity of experimentation necessary to generate the infinite number of derivatives recited in the claims and possibly screen same for activity, the lack of direction/guidance presented in the specification regarding which structural features are required in order to provide activity, the absence of working examples directed to same, the complex nature of the invention, the state of the prior art which establishes the unpredictability of the effects of mutation on protein structure and function, and the breadth of the claims which fail to recite any structural or functional limitations, undue experimentation would be required of the skilled artisan to make and/or use the claimed invention in its full scope.

Applicant argues that the claims encompass the use of a fragment that retains the binding activity with the corresponding S4-S5 cytoplasmic loop or amino-terminal inactivation region. However, the claims as written do not set forth the limitation wherein the biologically active fragment has such binding activity. The preamble of the claim sets forth that the method is for identifying compounds for the ability to inhibit binding of an intracellular region of an α-subunit of a voltage gated ion channel to an amino terminal inactivation region, however, the preamble is generally not accorded any patentable weight where it merely recites the purpose of a process or the intended use of a structure, and where the body of the claim does not depend on the preamble for completeness but, instead, the process steps or structural limitations are able to stand alone.

In re Hirao, 535 F.2d 67, 190 USPQ 15 (CCPA 1976). In In re Hirao, 535 F.2d 67, 190 USPQ 15 (CCPA 1976), the claim preamble set forth "A process for preparing foods and drinks sweetened mildly, and protected against discoloration, Streckler's reaction, and moisture absorption." The body of the claim recited two steps directed to the formation of high purity maltose and a third step of adding the maltose to foods and drinks as a sweetener. The court held that the preamble was only directed to the purpose of the process, the steps could stand alone and did not depend on the preamble for completeness. Here, the method steps do not require that the biologically active fragment retains binding activity, and since detailed information regarding the structural and functional requirements of the polypeptide fragment is lacking, it is unpredictable as to which variations, if any, meet the limitations of the claims. Applicant additionally argues that one of skill in the art can readily test whether the fragment can bind to the corresponding S4-S5 loop or inactivation region, however, Applicant is required to enable one of skill in the art to make and use the claimed invention, while the claims encompass methods using polypeptides which the specification only teaches one skilled in the art to test for functional variants to be used in the claimed method. It would require undue experimentation for one of skill in the art to make and use the claimed fragments, since the skilled artisan would have to first make polypeptide fragments, then test for function. Because the amino acid sequence of a polypeptide determines its structural and functional properties, and predictability of which amino acids can be substituted is extremely complex, accurate predictions of a polypeptide's structure from mere sequence data are limited. Thus, since Applicant has only taught how to test for polypeptide fragments, and has not taught how to make polypeptide fragments, it would require undue experimentation of one of skill in the art to practice the claimed method.

Claims 45-46 stand rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention, for reasons of record set forth in the Office Action of 8/24/2004. Applicant is directed to the Guidelines for the Examination of Patent Applications Under the 35 U.S.C. 112, ¶ 1 "Written Description" Requirement, Federal Register, Vol. 66, No. 4, pages 1099-1111, Friday January 5, 2001.

The rejection of record set forth that these are genus claims. The claims are drawn to a method of evaluating a compound for the ability to inhibit binding of an α-subunit intracellular receptor region of a voltage gated K channel to an amino-terminal inactivation region of a potassium channel protein, wherein the voltage gated channel proteins are Kv1.1 and Kvβ1, wherein the proteins are biologically active fragments of the proteins, thus, the claims encompass methods using variant proteins. The specification and claim do not indicate what distinguishing attributes shared by the members of the genus. The specification and claim do not place any limit on the number of amino acid substitutions, deletions, insertions and/or additions that may be

made to the proteins. Applicant argues that the claims are directed to the use of a biologically active fragment of an S4-S5 loop or an amino terminal inactivation region, and such a fragment can be readily determined. However, the written description requirement for a claimed genus may be satisfied through sufficient description of a representative number of species by actual reduction to practice, reduction to drawings, or by disclosure of relevant identifying characteristics, i.e. structure or other physical and/or chemical properties, by functional characteristics coupled with a known or disclosed correlation between structure and function structure, or by a combination of such identifying characteristics, sufficient to show the applicant was in possession of the claimed genus. In the instant case, the specification fails to provide sufficient descriptive information, such as definitive structural or functional features of the genus of polypeptide fragments used in the claimed method. There is no description of the conserved regions which are critical to the structure and function of the genus claimed. There is no description of the sites at which variability may be tolerated and there is no information regarding the relation of structure to function. Structural features that could distinguish the compounds in the genus from other seven transmembrane region compounds are missing from the disclosure. Furthermore, the prior art does not provide compensatory structural or correlative teachings sufficient to enable one of skill to isolate and identify the polypeptides encompassed: there is no guidance in the art as to what the defining characteristics of the polypeptides might be. Thus, no identifying characteristics or properties of the instant polypeptides are provided such that one of skill would be able to predictably identify the fragments which would function in the claimed method.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (e) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effects for purposes of this subsection of an application filed in the United States only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.

Claims 45-46, 50, 52-68 are rejected under 35 U.S.C. 102(e) as being anticipated by U.S. Patent No. 5,856,155 (Li).

The claims are directed to a method of evaluating a compound for the ability to inhibit binding of an α-subunit intracellular receptor region of a voltage gated K channel to an amino-terminal inactivation region of a potassium channel protein, wherein the voltage gated channel proteins are Kv1.1 and Kvβ1, wherein the first peptide comprises the S4-S5 looop and the second protein comprises the amino terminal inactivation region of a potassium channel α or β-subunit. The claims are anticipated because the '155 patent discloses a yeast two-hybrid system comprising a first vector containing nucleic acid sequences encoding a fusion protein of a DNA binding domain and a polypeptide consisting of the NAB and linking region of an alpha-subunit of a Shaker-like potassium ion channel, and a second vector containing nucleic acid sequences encoding a fusion protein of a transactivation domain and a polypeptide consisting of the NAB and linking region of an alpha-subunit of a Shaker-like potassium ion channel (column 4, lines 10-25). The alpha subunit is disclosed as being Kv1.4 (column 23, lines 10-25). The '155 patent further discloses methods of identification of compounds that inhibit the interaction (column 17, lines 20-65).

References

The Office will no longer be supplying paper copies of U.S. Patents cited in Office Actions. Applicant is advised that the cited U.S. patents and patent application publications are available for download via the Office's PAIR. As an alternate source, all U.S. patents and patent application publications are available on the USPTO web site (www.uspto.gov), from the Office of Public Records and from commercial sources. Applicant may direct inquiries about the use of the Office's PAIR system to the Electronic Business Center (EBC) at http://www.uspto.gov/ebc/index.html or 1-866-217-9197.

Conclusion

No claim is allowed.

Advisory Information

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Joseph Murphy whose telephone number is (571) 272-0877. The examiner can normally be reached Monday through Friday from 7:30 am to 5:00 pm. A message may be left on the examiner's voice mail service. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Tony Caputa, can be reached on (571) 272-0829.

The fax number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR

system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Joseph F. Murphy, Ph. D.
Patent Examiner
Art Unit 1646
January 27, 2005

JOSEPH MURPHY
PATENT EXAMINER